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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,879	03/18/2004	Sergio Abrignani	2300-0336.10	7660

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,879	ABRIGNANI, SERGIO	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/011,910.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 18, and 21-23 are pending and under consideration. Claims 1-17, and 19-20 were cancelled, and claims 21-23 added in the preliminary amendment filed on March 18, 2004.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on March 18, 2004 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

3. It is noted that the Darzynkiewicz et al. reference cited in the IDS has been crossed off. This is because the reference has not properly been submitted to the office as no copy of the reference has been provided. See, page 2 of the Office Action mailed on September 14, 1999 in parent application 09/011910 (indicating that no legible copy of the reference had been submitted to the Office with the IDS). The reference has therefore not been considered.

Claim Rejections - 35 USC § 101

4. Claims 18 and 21-23 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

These claims read on methods of identifying compounds capable of binding to the Hepatitis C virus (HCV) region responsible for binding to a host cell. The claimed methods

involve screening the test compounds for their ability to bind to a protein having a molecular weight of about 24kd so as to identify compounds that bind to the E2 protein of HCV.

However, the 24kd protein referred to in the claims is disclosed in the application as (probably) a cellular transmembrane receptor protein from human cells which itself binds to the HCV E2 protein. See, App. pages 2-3. Thus, the methods described in the claims are identifying compounds that bind to a cellular protein, and not to a viral protein. Further, the application provides no reason to believe that the ability of a target compound to bind to the target cellular protein (itself a target of HCV binding) would be indicative of the compounds ability to bind HCV. Rather, the claims appear to be identifying compounds that could potentially compete with the HCV E2 proteins for binding to the cellular protein. Thus, the claimed methods are not credible in that they appear to describe an inoperable method of identifying compounds that bind to HCV.

Claim 18 and 21-23 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 18 and 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a method indicating how the ability to bind to the 24kd protein relates to the compounds ability to bind to HCV. The omitted step is necessary to describe how the indicated method step relates to the intended functionality of the method.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 18 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being (for the purposes of this rejection) enabling for the claimed methods wherein the protein to which binding is being screened is the 24kd protein that binds to the HCV E2 protein, does not reasonably provide enablement for methods using any "functionally equivalent" or fragment thereof thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are rejected for two reasons. First, the Applicant has not established that any "functionally equivalent" variant or fragment would be useful in the claimed invention. Second, the Applicant has not enabled the making and use of any "functionally equivalent" fragment or variant thereof.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The claims are drawn to a method of identifying compounds through their ability to bind to a compound having a molecular weight or 24kd and that bind the HCV E2 protein, wherein such proteins are isolated from cells capable of binding to the HCV E2 protein (i.e. human cells and chimpanzee cells). The application provides neither a means of identifying such proteins other than through their isolation as described above, or an identification of the proteins' activities other than binding to the HCV E2 protein. The claims are also not limited the use of fragments or variants that have the ability of the 24kd protein to bind to the HCV E2 protein. Rather, they are drawn to methods of using any "functionally equivalent" variant or fragment thereof. This failure to limit the claims to variants and fragments with E2 binding ability leads to two problems. First, it is not clear what other functions may be performed by these molecules as the application has not provided any identification of functions (other than E2 binding) that performed by the proteins in the human or chimp cells from which they are isolated.

Additionally, the Applicant has not demonstrated that any function other than E2 binding would be useful in the claimed methods.

However, even if the claims were limited to variants and fragments with E2 binding ability, the claims would still not be fully enabled. The application provides no guidance as to what variants or fragments may be considered functional equivalents of the indicated proteins as there is no description as to what features of the proteins are required for the HCV E2 binding function. There is no description of the protein's sequence' or what residues within the sequence are required for E2 binding. Nor is there any identification of any structural feature that enables those in the art to identify proteins that are "functionally equivalent" thereto.

Because the claims are directed to the use of variants of isolated proteins, the art surrounding the invention is that of protein sequence manipulation. References in this art, such as the Bowie et al. reference cited in the IDS, indicate that the art is unpredictable. Bowie teaches that, while proteins tend to be tolerant to some amount of sequence mutation, the effects that any particular mutation would have are generally unknown. The reference further indicates that the unpredictability may be reduced by teachings relating to the relationship between the target protein residue and the functional and structural characteristics of the protein.

As indicated above, there are no such teachings relating to the relationship between the protein sequence and the protein function. The Applicant has provided no identification of the sequences or structure of the protein itself, much less any identification of what residues within it may or may not be required for its ability to bind to the HCV protein. Nor are there any variants or fragments of the protein disclosed from which such teachings may be drawn. Thus, in view of the lack of guidance towards proteins other than the isolated protein itself, the Applicant has not

enabled the practice of the claimed methods to the extent that it reads on the use of these functional equivalents.

9. Claims 18 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims have been described above. The claims read on methods of using any "protein having a molecular weight of about 24kd and which binds to the E2 protein of hepatitis C virus" or fragments or variants thereof, for the identification of compounds that bind to HCV. The Applicant has however provided only a single example of such proteins. The proteins are indicated in the specification to be proteins with the indicated chemical and functional features (molecular weight and E2 binding capability), and which may be isolated from human or chimpanzee cells. However, the claims are not limited to methods wherein the proteins are of human or chimpanzee origin. They read on methods involving the use of any proteins with the correct molecular weight that can bind the HCV E2 protein.

However, the Federal Circuit has stated that, to satisfy the written description requirement, the Applicant must provide a description of the claimed genus by providing, for example, "a representative number of species" actually reduced to practice," or by identifying a set of "functional characteristics coupled with a known or disclosed correlation between function and structure." Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. In either case, the court

stated, "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus."

In the present case, the claims may include other proteins with the indicated chemical and functional characteristics that are not isolated from human or chimpanzee cells. However, there is no description of any such proteins, or any described correlation between a structure and desired function, that would allow those in the art to easily identify other members of the groups of proteins that may be used in the claimed methods. Further, the application specifically teaches that the proteins used in the claimed methods, while ubiquitous in human cells and present in chimpanzees, are not to be found in any other mammals. Page 9, lines 27-29. Thus, the Applicant has not provided sufficient written description to support the use of any protein with the indicated molecular weight and binding activity. See e.g., Sasaki et al., (indicating that other molecules on human cells may act as HCV receptors as well). The Applicant has provided written description only for those proteins that may be found in the cells of the two indicated primates.

The claims additionally read on the use of fragments and variants of the proteins isolated from those cells. However, the application provides no examples of any such fragments or variants, or any means of identifying such molecules other than by function (i.e. as functional equivalents of the 24 kd protein). Because the application discloses neither a sufficient number of species falling within this genus of fragments of variants to demonstrate possession, nor a means other than by function to identify the members of this genus of molecules, the Applicant has provided insufficient description for methods using such functionally equivalent variants and fragments.

For the reasons above, the Applicant has not provided sufficient written description for the claimed methods to the extent that they exceed the use the 24 kd of proteins that bind the HCV E2 protein, and that are isolated from human or chimpanzee cells.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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10/15/04